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**1. Contingency Preparedness:** Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan.

**2. Rapid Identification of Matched Donors :** Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event.

**3. Immunogenetic Studies:** Increase understanding of the immunologic factors important in HSC transplantation.

**4. Clinical Research in Transplantation:** Create a platform that facilitates multicenter collaboration and data management.

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Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes

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# QUARTER PROGRESS REPORT

## Development of Medical Technology for Contingency Response to Marrow Toxic Agents

July 01, 2007 through September 30, 2007

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<b>IIA. Contingency Preparedness – Hypothesis 1:</b> Recovery of casualties with significant myelosuppression following radiation or chemical exposure is optimal when care plans are designed and implemented by transplant physicians	
<b>IIA.1.1 Aim 1:</b> Secure Interest of Transplant Physicians	<p><b>Period 4 Activity:</b></p> <p><b>Funding provided by both 0859 and 0704 contracts this quarter:</b></p> <ul style="list-style-type: none"> <li>• Conducted physician education seminar titled: <u>Medical and Organizational Challenges Resulting from a Radiological/Nuclear Emergency Seminar</u> radiological/nuclear emergency. <ul style="list-style-type: none"> <li>○ Seminar was held on September 25, 2007 in Bethesda, MD.</li> <li>○ The Medical College of Wisconsin provided 6 CME credits for attendees</li> <li>○ 132 people advance registered to attend, and 17 people registered the day of the seminar</li> <li>○ Topics and key speakers include: <ul style="list-style-type: none"> <li>▪ Threat Assessment : Brooke Buddemeier, C.H.P. - Lawrence Livermore National Laboratory</li> <li>▪ A Possible Scenario for Nuclear Casualties: Carl Curling, Sc.D. - Institute for Defense Analysis</li> <li>▪ Lessons from the Past: Chernobyl: Alla Shapiro, M.D. - Food and Drug Administration</li> <li>▪ Mass Casualty Event Case Studies: <ul style="list-style-type: none"> <li>• David Rutstein, M.D. - Health and Human Services</li> <li>• Nelson Valverde, M.D. - State University of Rio de Janeiro</li> </ul> </li> </ul> </li> </ul> </li> <li>▪ Introduction to Radiation Biology: Michael Robbins, Ph.D. - Wake Forest University School of Medicine</li> <li>▪ Biodosimetry: Albert Wiley, M.D. - REAC/TS &amp; WHO Collaborating Center at Oak Ridge</li> <li>▪ ARS Skin syndrome: Viktor Meienke, M.D. - Bundeswehr Institute of Radiobiology</li> <li>▪ ARS Hematologic syndrome: Theodor Fliedner, M.D. – Ulm University</li> <li>▪ ARS Gastrointestinal syndrome: Martin Hauer-Jensen, M.D. - University of Arkansas for Medical Sciences</li> <li>▪ Radiation-induced Brain Injury: Michael Robbins, Ph.D. - Wake Forest University School of Medicine</li> <li>▪ Multi-organ Failure : Marc Benderitter, M.D. - Institut De Radioprotection et de Surete Nucleaire</li> <li>▪ National Response Process - the HHS "Playbook": C. Norman Coleman, M.D. - National Institute</li> </ul>

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	<p>of Health</p> <ul style="list-style-type: none"> <li>▪ New Approaches to Therapy Next Generation Medical Countermeasures: Nelson Chao, M.D. - Duke University</li> <li>• Distributed training and reference materials to new RITN centers:             <ul style="list-style-type: none"> <li>○ Copy of the “Medical Management of Radiation Accidents: Manual on the Acute Radiation Syndrome” a.k.a. the ‘Fliedner protocol’</li> <li>○ CDC training DVD “Medical Response to Nuclear and Radiological Terrorism”</li> </ul> </li> </ul>
<b>IIA.1.2 Aim 2:</b> GCSF in Radiation Exposure	<p><b>Period 4 Activity:</b></p> <p>No activity this period.</p>
<b>IIA.1 3 Aim 3:</b> Patient Assessment Guidelines	<p><b>Period 4 Activity:</b></p> <p>Cord blood bank recruitment registered 3,773 new cords and made them available for searches. Cord blood bank conversion continued with CBB 192, Singapore, who went live with more than 500 cords. The new banks Sheba (Israel) and Gift of Life are in the process of mapping their data, while NMDP developers are creating conversion programs. These banks are expected to go live in the near future.</p> <p>To support new FDA regulations, the following changes were made to <b>CORD Link Web</b>:</p> <ul style="list-style-type: none"> <li>○ New N2F and GFC Maternal Risk Questionnaires and Validation Protocols.</li> <li>○ New N2E Maternal Demographic and CBU IDM forms and Validation Protocols.</li> </ul> <p>To support the cord recruitment funding programs the following features were added:</p> <ul style="list-style-type: none"> <li>○ Funding Goal Management - Allows NMDP and CBBs view and manage CORD Funding goals.</li> <li>○ Funding Data Synch - Allows NMDP IT staff to synchronize funding data between systems.</li> <li>○ Funding Data Download - Internal tool used by NMDP staff to allow appropriate CORD funding personnel to retrieve detail funding data for use in CORD Funding selection.</li> </ul> <p>The following changes were made to the Centralized Repository Information System (<b>CRIS Link</b>): In the past quarter, CRIS Link was updated allowing repository staff to enter drive information for recruitment samples. This information confirms sample storage back to the donor center. The donor center can track samples that were</p>



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	<p>processed by the Repository for a given drive. This information is summarized over storage sets that share the same drive key, and groups all drive keys together with cumulative totals.</p> <p>The following changes were made to the Research Sample Repository software: Development has commenced on the related pairs repository functionality for the research repository. This functionality will allow the research repository to assign donor and recipient ID's to transplant center that will be used to track related transplant activity at these centers. This feature is scheduled to be released in conjunction with FormsNet 2.0 in the 4th quarter of 2007.</p>
<b>IIA 1.4 Aim 4:</b> National Data Collection Model	<p><b>Period 4 Activity:</b></p> <p>No activity this period.</p>
<b>IIA. Contingency Preparedness – Hypothesis 2:</b> Coordination of the care of casualties who will require hematopoietic support will be essential in a contingency situation.	
<b>IIA.2.1 Aim 1:</b> Contingency Response Network	<p><b>Period 4 Activity:</b></p> <p><b>Exercises:</b></p> <ul style="list-style-type: none"> <li>• Conducted an orientation exercise and a tabletop exercise with Emergency Response Team staff.</li> <li>• This training was in preparation for participating in the federal exercise Top Officials 4 (TOPOFF 4).</li> <li>• Continued coordinated with HHS and the ABBB Inter-organizational Task Force on Domestic Disasters and Acts of Terrorism for RITNs participation in TOPOFF 4 in October.</li> </ul> <p><b>Meetings:</b></p> <ul style="list-style-type: none"> <li>• Held nine (9) conference calls with RITN centers to assist in completion of milestones and to improve integration into the network.</li> <li>• Reviewed submitted RITN standard operating procedures.</li> <li>• Graded 530 Basic Radiation Training exams submitted by RITN centers.</li> </ul> <p><b>Communications:</b></p> <ul style="list-style-type: none"> <li>• Distributed additional satellite telephones; a total of 56 phones are distributed to RITN centers.</li> <li>• Temporarily issued a satellite telephone to DC 109 in Puerto Rico as a backup communication option due</li> </ul>

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	<p>to hurricane season.</p> <ul style="list-style-type: none"> <li>• Distributed additional GETS cards; a total of 126 cards are issued to NMDP staff and RITN centers.</li> <li>• Conducted communication tests with the NMDP Network (August), a GETS card user test (July), a satellite telephone test (July), and used the bulk telephonic notification system to notify NMDP staff in August related to the I-35W bridge collapse.</li> </ul> <p><b><u>Funding provided by both 0859 and 0704 contracts this quarter:</u></b></p> <p><b>RITN development:</b></p> <ul style="list-style-type: none"> <li>• Completed the signing of 53 centers to participate in RITN:             <ul style="list-style-type: none"> <li>○ 37 transplant centers</li> <li>○ 9 donor centers</li> <li>○ 7 cord blood banks</li> </ul> </li> </ul>
<b>IIA.2.2 Aim 2:</b> Sibling Typing Standard Operating Procedures	<p><b>Period 4 Activity:</b></p> <p>No activity this period.</p>
<b>IIA. Contingency Preparedness – Hypothesis 3:</b> NMDP's critical information technology infrastructure must remain operational during contingency situations that directly affect the Coordinating Center.	
<b>IIA.3.1 Aim 1:</b> I.S. Disaster Recovery	<p><b>Period 4 Activity:</b></p> <p>The NMDP's STAR Link Disaster Recovery hardware was upgraded in August 2007 as part of the STAR Link production hardware replacement. The new hardware is identical to the production systems. Production data is being replicated using log shipping technology to our DR site located in Leawood KS. This has reduced the recovery time for the STAR Link environment since we do not need to load all of the data from tape.</p> <p><b>Business Continuity Planning:</b></p> <ul style="list-style-type: none"> <li>• Critical Staff Recovery Site (CSRS) development:             <ul style="list-style-type: none"> <li>○ Presented detailed CSRS options to NMDP CMO, CFO, and CIO.</li> <li>○ Officers identified preferred option that will be an NMDP facility in the Twin Cities area that houses</li> </ul> </li> </ul>



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	<p>NMDP staff daily and has space for critical staff to operate in the event of a Coordinating Center disruption.</p> <ul style="list-style-type: none"> <li>○ Established an ongoing monthly meeting with the CIO and CFO to keep CSRS project moving forward and to ensure an interim plan is implemented.</li> <li>● Further developed the coordinating center business impact analysis and hazard assessment to provide basis for updated business continuity plan.</li> </ul>
<b>IIB. Rapid Identification of Matched Donors – Hypothesis 1:</b> Increasing the resolution and quality of the HLA testing of volunteers on the registry will speed donor selection.	
<b>IIB.1.1 Aim 1:</b> Increase Registry Diversity	<p><b>Period 4 Activity:</b></p> <ul style="list-style-type: none"> <li>● Completed testing of 21,006 newly recruited volunteer donors.</li> <li>● Blind quality control testing error rate average was 0.08% satisfying the project requirement of <math>\leq 1.5\%</math>.</li> <li>● Testing completion rate was 97%, meeting the project requirement of 85% of typing results reported within 14 days from shipment of samples.</li> <li>● ABDR contracts extended to March 30, 2008</li> <li>● 1 contract laboratory added to increase total sample capacity due to increased overall recruitment.</li> <li>● Preliminary work has been completed for the RFP scheduled to be released in November, 2007.</li> </ul> <p>Starting next quarter, the NMDP Center for Support Services (CSS) group will perform all donor entry activities. To support increased workload the following features were implemented:</p> <ul style="list-style-type: none"> <li>● Pending donor workflow management screens were created that allow the CSS group to organize and assign donor follow-up where there are missing data on the consent forms.</li> <li>● STAR Link was upgraded with an online health history questionnaire for donor center staff. This feature is being considered for the Do It Yourself donor (DIY) application that would allow donors to complete health history questionnaire forms during the search processes. This functionality would also enable automated contact with potential donors in FY 2008 for the pre-search project.</li> </ul>
<b>IIB.1.2 Aim 2:</b> Evaluate HLA-DRB1 High Res typing	<p><b>Period 4 Activity:</b></p> <p>This task is closed.</p>

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<b>IIB.1.3 Aim 3:</b> Evaluate HLA-C Typing of Donors	<b>Period 4 Activity:</b> This task is closed.
<b>IIB.1.4 Aim 4:</b> Evaluate Buccal Swabs	<b>Period 4 Activity:</b> <b>Alternative cell type for blind Quality Control swab samples</b> <ul style="list-style-type: none"> <li>B-LCL swabs have been created from 17 different cell lines. These new QC swabs have been sent to all 6 contract labs, and will soon be the sole QC swab type, replacing DNA dipped swabs and "Real" buccal swabs currently collected by QC donors at the Coordinating Center in Minneapolis.</li> <li>Additional B-LCL cell lines are being selected for swab creation to increase the variety of HLA types.</li> </ul> <b>Sample Storage Research Study (SSRS)</b> <ul style="list-style-type: none"> <li>Objective: Evaluate the usefulness of donor samples, stored over time, for HLA testing.</li> <li>The study began on September 13, 2007 and enrolled 32 current QC donors. Whole blood and buccal swab samples were collected from each donor and transferred to the NMDP Repository for storage. Baseline samples were sent for intermediate and high resolution HLA testing and evaluation of DNA quality and quantity on September 18, 2007. Results are expected early next quarter</li> <li>The next testing time point is September, 2008.</li> </ul>
<b>IIB 1.5 Aim 5:</b> Enhancing HLA Data for Selected Donors	<b>Period 4 Activity:</b> <b>Replacement Donor Pilot Study</b> <ul style="list-style-type: none"> <li>A total of 1515 patient searches with active work-up requests were reviewed by Scientific Services staff.</li> <li>For those work-up requests where there was not one or more equivalently HLA matched replacement donors available, up to 5 potentially matched donors were selected (when available) for prospective high resolution HLA A, B, C and DRB1 typing. There were 480 potentially matched donors selected for prospective typing over the course of the study. Approximately 95 % of these donors had stored samples in the NMDP Repository.</li> <li>Donor contacts were made to confirm availability, provide education, conduct an abbreviated medical history assessment and, if necessary, to send out a buccal swab kit when a Repository sample was not available. The NMDP Call-Back Unit processed 429 of the donor contacts, and transferred 51 donors to</li> </ul>



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	<p>participating Donor Centers (n=9) performing their own donor contacts for this pilot project.</p> <ul style="list-style-type: none"> <li>• 208 donors were confirmed available, and samples were shipped to the project laboratory for prospective HLA typing. All typing results were completed in the specified turnaround time.</li> <li>• Twelve donors were activated for either a patient-directed customized typing request or for Confirmatory Typing (CT) before a prospective typing started.</li> <li>• The remaining donor contacts were resolved as follows: 84 Not Interested (NI), 40 Medically Deferred (DD), 46 Temporarily Unavailable (TU) and 90 Unable to Contact (UC).</li> <li>• Data analysis has begun, with a final report and recommendations to be completed in the next quarter.</li> </ul> <p><b>Optimum Donor Pilot Study</b></p> <ul style="list-style-type: none"> <li>• A strategy was developed to evaluate the patient phenotypes that have been submitted to the NMDP over the years for a donor search (referring physician, preliminary, formal). The phenotypes were categorized and potential donor coverage was assessed in the overall NMDP Registry and the donors sub-grouped to show the contributions by the US donor pool, the DoD donor pool and the International donor component of the Registry.</li> <li>• Only patient phenotypes with one or more potential donor matches in the Registry were included (singletons were excluded). The donors were grouped into two categories; high resolution and/or low-intermediate resolution typing at HLA-A, B &amp; DRB1. Patient phenotypes with no potential donors with high resolution typing were identified. Search reports were then run to identify younger male or female donors (US only, non-DoD) for prospective high-resolution typing.</li> <li>• 665 donors were selected for prospective typing. Donor contacts were initiated to confirm availability, provide education, conduct an abbreviated medical history assessment and if necessary, to send out a buccal swab kit when a Repository sample was not available. The NMDP Call-Back Unit initiated 589 donor contacts, and provided information on the remaining 76 donors to participating Donor Centers (n=9) performing their own donor contacts for this pilot project.</li> <li>• 181 donor samples have been selected and shipped to the project laboratory for prospective HLA typing and all results due during the quarter (N=64) were completed in the specified turnaround time.</li> </ul>
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<b>IIB. Rapid Identification of Matched Donors – Hypothesis 2:</b> Primary DNA typing data can be used within the registry to improve the quality and resolution of volunteer donor HLA assignments.	
<b>IIB 2.1 Aim 1:</b> Collection of Primary Data	<b>Period 4 Activity:</b> A new version of the software to process laboratory typing results electronically (HML) was implemented that allows the data to be sent as genotype lists. This allows laboratories to report data as it comes from their analysis software directly to the NMDP without requiring the step of compressing it to multiple allele codes which is time consuming and introduces ambiguity.
<b>IIB 2.2 Aim 2:</b> Validation of Logic of Primary Data	<b>Period 4 Activity:</b> This task is closed.
<b>IIB 2.3 Aim 3:</b> Reinterpretation of Primary Data	<b>Period 4 Activity:</b> This task is closed.
<b>IIB 2.4 Aim 4:</b> Genotype Lists & Matching Algorithm	<b>Period 4 Activity:</b> The software development for the 2 <sup>nd</sup> phase of the HapLogic™ algorithm was completed during the past quarter. This includes production of allele match probabilities for HLA-C and HLA-DQB1 as well as a re-definition of HLA match according to the antigen recognition site (ARS) so that HLA types that match within this region (e.g. Exons 2 & 3 for Class I and Exon 2 for Class II) will be considered an allele match. This new version of the algorithm also includes a complete update of all haplotype frequencies based on the minority random pool typing.
<b>IIB. Rapid Identification of Matched Donors – Hypothesis 3:</b> Registry data on HLA allele and haplotype frequencies and on the nuances of HLA typing can be used to design computer algorithms to predict the best matched donor.	
<b>IIB.3.1 Aim 1:</b> Phase I of EM Haplotype Logic	<b>Period 4 Activity:</b> The development of the second phase of HapLogic™ (C and DQ predictions) included a comprehensive retrospective validation where all informative donor retypings (CT or HR) were analyzed to compare the prediction by HapLogic to the actual results. Scientific Services and Bioinformatics staff categorized and began



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	analysis of the data generated from the validation and the final report is expected to be completed in the next quarter.
<b>IIB 3.2 Aim 2:</b> Enhancement of EM Algorithm	<p><b>Period 4 Activity:</b></p> <p>Two typing programs were initiated that will provide additional haplotype frequency data for the enhanced HapLogic II algorithm. The typings utilized randomly selected minority adult donor samples and recruitment stage Cord Blood Unit samples. Two laboratories were selected to provide the HLA typing of these samples at high resolution for HLA-A, B, C, DRB1/3/4/5 and DQB1.</p> <p>Approximately 2200 prospective minority donor samples were shipped to the laboratories during August and September. The target enrollment for newly recruited cord blood units (CBUs) is 825 which will ship between July-October. HLA results for both programs will be completed in October.</p> <p>A second objective of CBU typing is to evaluate the utilization of the high resolution typed CBUs versus the standard recruitment typed CBUs to determine whether the availability of high resolution typing at recruitment affects CBU selection. And time to transplant.</p> <p>The manuscript "High-resolution HLA alleles and haplotypes in the United States population" was published in the September issue of Human Immunology. This study provides 1-5 locus haplotype frequencies in the main US ethnic groups. The frequency tables are available for download at <a href="http://bioinformatics.nmdp.org/haplotype2006">bioinformatics.nmdp.org/haplotype2006</a></p> <p>A total of seven abstracts were presented at the ASHI meeting in Minneapolis reporting on haplotype frequency analysis work performed under this aim.</p> <ol style="list-style-type: none"> <li>1) NEMO – High Resolution HLA-A, -B, -DRB1 haplotype frequencies from the whole DNA-probe typed NMDP registry</li> <li>2) Subtraction: deducing source population HLA composition in US ethnic groups</li> <li>3) Unsupervised clustering of individuals into HLA genetic clusters using Hardy-Weinberg deviation</li> <li>4) HLA frequency analysis of Brazilian ethnic groups and comparison to US ethnic groups</li> <li>5) HLA frequencies and genetic distances between Ashkenazi and non-Ashkenazi Israeli Jews</li> <li>6) HLA population differentiation and inference of disease predisposition: the case of cALL</li> </ol>

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	7) HLA as an Ancestry Informative Marker (AIM). Three of these abstracts (Subtraction, Clustering and Israel) were also accepted for presentation at the American Society of Human Genetics (ASHG) meeting in October.
<b>IIB 3.3 Aim 3:</b> Optimal Registry Size Analysis	<b>Period 4 Activity:</b> A meeting has been scheduled for Monday Dec 3 <sup>rd</sup> , 2007 in Chicago for a panel of population genetics experts to consider the problem of projecting match rates at high-resolution. The meeting will generate recommendations for how to proceed with the analysis in support of this aim.
<b>IIB 3.4 Aim 4:</b> Target Under-represented Phenotypes	<b>Period 4 Activity:</b> An abstract was submitted and accepted to the American Society of Human Genetics (ASHG) meeting in October describing the NMDP GeoCoding project. The development of a set of tools to suggest geographical targets for recruitment for a particular genotype are being developed in response to inquiries from the network.
<b>IIB 3.5 Aim 5:</b> Bioinformatics Web Site	<b>Period 4 Activity:</b> The haplotype frequencies accompanying the manuscript published in Human Immunology (described in IIB3.4 Aim 2) were made publicly available on the Bioinformatics Web site (bioinformatics.nmdp.org/haplotype2006). The data are available in pdf format or xls (spreadsheets).
<b>IIB 3.6 Aim 6:</b> Consultants to Improve Algorithm	<b>Period 4 Activity:</b> No activity this period.
<b>IIB. Rapid Identification of Matched Donors – Hypothesis 4:</b> Reducing the time and effort required to identify closely matched donors for patients in urgent need of HSC transplants will improve access to transplantation and patient survival in the context of a contingency response and routine patient care.	
<b>IIB.4.1 Aim 1:</b> Expand Network Communications	<b>Period 4 Activity:</b> <b>Continued the support for QA testing and monitoring of:</b> <ul style="list-style-type: none"> <li>Internal versions of Search Assistance Tools, MultiCord and HaploSTATs applications by search strategy staff.</li> </ul>



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	<ul style="list-style-type: none"> <li>• External versions of SAT and MultiCord applications.</li> </ul> <p><b>SEARCH Link and TRANS Link applications upgrades:</b></p> <ul style="list-style-type: none"> <li>• HapLogic, the NMDP's matching algorithm, was enhanced to calculate mismatches between patients and cords for the antigen and the allele levels at HLA-DRB1. This change was approved by both the Cord Blood Committee and the Histocompatibility Committee. The Cord search reports, SEARCH Link, and TRANS Link applications were upgraded to display the new cord match categories of 3/6 or 2/6, since units that previously displayed on the cord list may now be in the 3/6 or 2/6 match category.</li> <li>• The donor sort order was enhanced to include the donor's age, which is an important selection criterion for transplant centers. The donor sort order is listed below:             <ul style="list-style-type: none"> <li>○ Match Category</li> <li>○ Pr (6) = %</li> <li>○ Pr (5) = %</li> <li>○ Donor's Age (Ascending – youngest to oldest)</li> <li>○ Donor ID (Ascending – lowest to highest)</li> </ul> </li> <li>• To comply with FDA Final Eligibility Guidelines the following changes were made:             <ul style="list-style-type: none"> <li>○ Two new form validation protocols, Grandfather C (GFC) and version N2F were added to the Maternal Risk Questionnaire (MRQ).</li> <li>○ The N2F form validation protocol required changes to screens and search reports</li> <li>○ The GFC form includes the same questions as the N2F. However, the GFC form allows the banks two more selection options per question: (1) <i>Bank did not ask</i>; and (2) <i>Mother did not answer</i>. The GFC form will be utilized in the Grandfather 2 (GF2) cord validation protocols only.</li> <li>○ N2E IDM form validation protocol contains three new tests: (1) <i>Anti-CMV (Total)</i>; (2) <i>Chagas EIA</i>; and (3) <i>RIPA (confirmatory)</i> (Chagas confirmatory test).                 <ul style="list-style-type: none"> <li>▪ Interpretation information for infectious disease marker (IDM) testing is available on the NMDP Network Website</li> </ul> </li> <li>○ To improve operational efficiencies for the Transplant Center and the Search and Transplant Services department,                 <ul style="list-style-type: none"> <li>▪ Two new fields were added: (1) <i>Funded</i> indicating whether or not the cord is funded; and (2)</li> </ul> </li> </ul> </li> </ul>
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	<p><i>NCBI</i> indicating whether or not the cord is part of the National Cord Blood Inventory (NCBI).</p> <ul style="list-style-type: none"> <li>Two new filters in Custom criteria were added for Match Probability (%) at HLA-DQB1 and C loci to prepare for HapLogic phase II.</li> </ul> <p><b>STAR II upgrades:</b></p> <ul style="list-style-type: none"> <li>Release STAR2_043 2007-07-09           <ul style="list-style-type: none"> <li>Support for flexible id assignment to Cord blood units to support Cord sorting.</li> <li>STAR Link XML transaction format enhancements.</li> </ul> </li> <li>Release STAR2_044 2007-07-19           <ul style="list-style-type: none"> <li>Support for new Cord IDM and Maternal Risk validation protocols.               <ul style="list-style-type: none"> <li>Support additional database and transaction fields.</li> <li>Support new rules for new protocols.</li> </ul> </li> </ul> </li> <li>Release STAR2_045 2007-09-12           <ul style="list-style-type: none"> <li>Move support for STAR Link donor transfer from STAR to STAR2. Allows donor transfers to take place in hours where previously it would have taken days.</li> <li>Support for new high resolution typing projects.</li> </ul> </li> </ul>
<b>IIB.4.2 Aim 2:</b> Central Contingency Management	<p><b>Period 4 Activity:</b></p> <p>Provided awareness and education of the Custom Search Support (CSS) service with presentation of an informational webinar for the TC network. This same presentation will be given at the NMDP Council Meeting next quarter. Work progressed towards a process for the use of CSS for compassionate requests.</p>
<p><b>IIC. Immunogenetic Studies – Hypothesis 1:</b> HLA mismatches may differ in their impact on transplant outcome, therefore, it is important to identify and quantify the influence of specific HLA mismatches. In contingency situations it will not be possible to delay transplant until a perfectly matched donor can be found.</p>	
<b>IIC.1.1 Aim 1:</b> Donor Recipient Pair Project	<p><b>Period 4 Activity:</b></p> <ul style="list-style-type: none"> <li>Typing of the 500 donor/recipient pair samples constituting Sample Group (SG) 17 was completed August 31, 2007. Discrepancy and no make analysis are underway.</li> </ul>



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	<ul style="list-style-type: none"> <li>• Typing of the 425 donor/recipient and 75 cord/recipient pair samples constituting SG18 began in September, 2007. The period of performance for SG18 is from September 1 to December 31, 2007.</li> </ul>
<b>IIC. Immunogenetic Studies – Hypothesis 2:</b> Even when patient and donor are HLA matched, GVHD occurs so other loci may play a role.	
<b>IIC 2.1 Aim 1:</b> Analysis of non-HLA loci	<p><b>Period 4 Activity:</b></p> <ul style="list-style-type: none"> <li>• Reporting of data for Phase 3 of the High Resolution KIR Typing Pilot Project was completed on September 30, 2007. All fourteen KIR loci have been typed.</li> <li>• Development of the next phase of the project is in process and will be completed early next quarter.</li> <li>• Discrepancy, ambiguity and no make analysis and resolution of Phase 1, 2 and 3 was ongoing.</li> <li>• Two abstracts were accepted for poster presentation at the 2007 ASHI annual meeting occurring October 8, 2007.</li> <li>• The Scientific Services and Bioinformatics departments continue to collaborate on the design and development of the Immunobiology Projects Results (IPR) database and tools to support immunogenetic testing projects.</li> <li>• Pilot project results for 12 KIR loci (2DL1-5, 2DS2,3, and 5, 3DL1-3 and 3DS1) were loaded into the IPR database and comparison and processing analysis was performed. Discrepancy and ambiguity data can now be extracted from the data base.</li> </ul> <p>During the past quarter there has been significant progress on the development of the new IPR (Immunobiology Project Results) database application. In early July, the team started Phase I of the project which consists of the following 3 items:</p> <ol style="list-style-type: none"> <li>1) KIR data import</li> <li>2) Development of the comparison/processing code to identify ambiguities/discrepancies</li> <li>3) Development of the review/resolution tools used to analyze/review the data.</li> </ol> <p>The IPR team has completed the KIR data import and developed the comparison/processing code. At present, the analysis and business requirements document for the review/resolution tools are complete. The technical</p>

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	<p>specifications document for these tools is in progress and development is scheduled for completion next quarter. Reporting of data for Phase 3 of the High Resolution KIR Typing Pilot Project was completed on September 30, 2007. The data from the first three phases of the NMDP donor KIR typing project was loaded into the IPR database. Preliminary discrepancy analysis was performed and haplotype frequency analysis of the consistent (non-discrepant) results has been initiated. Development of the next phase of the project is in process and will be completed early next quarter.</p> <p>Two abstracts were accepted for poster presentations at the ASHI annual meeting in October 23, 2007:</p> <ul style="list-style-type: none"> <li>• Description of the data reporting format developed in collaboration with the NIH PPG group at the University of Minnesota and Stanford ("A community standard reporting format for KIR genotyping data").</li> <li>• Description of the high resolution sequence based typing methods used in the NMDP High Resolution KIR Typing Pilot Project in collaboration with the three contract laboratories ("Sequence-based typing of KIR genes")</li> </ul>
<b>IIC 2.2 Aim 2:</b> Related Pairs Research Repository	<p><b>Period 4 Activity:</b></p> <ul style="list-style-type: none"> <li>• Sample collection will begin with the release of FormsNet 2.0 and the updated CIBMTR/NMDP data collection forms for support of the SCTOD. A formal release date is scheduled for announcement next quarter.</li> <li>• Printing of the related sample labels was completed and will be distributed to the seven pilot centers early next quarter.</li> <li>• NMDP Scientific Services, Bioinformatics and IT staff continued work on the modifications to the Repository inventory software and database to facilitate the receipt, processing, storage and retrieval of the related samples.</li> </ul> <p>NMDP Scientific Services, Bioinformatics and IT staff continued work on the modifications to the Repository inventory software and database to facilitate the receipt, processing, storage and retrieval of the related samples. During the past quarter the Research Repository team has made significant progress on the development of the following new tools within the Research Repository database application.</p>



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	<ol style="list-style-type: none"> <li>1) The Vial Inventory Tool has been developed, testing and bug fixes are complete. This tool is now in use.</li> <li>2) The Queue Management tool technical specification document is complete.</li> <li>3) The Pick Management Review tool business requirements document and technical specification document are complete.</li> <li>4) The Pick Management/Customer Pick tool business requirements document and technical specifications document are complete.</li> </ol> <p>Related pair sample collection will begin with the release of FormsNet 2.0 and the updated CIBMTR/NMDP data collection forms for support of the SCTOD. A formal release date is scheduled for announcement next quarter.</p>
<b>IID. Clinical Research in Transplantation – Hypothesis 1: Clinical research in transplantation improves transplant outcomes and supports preparedness for a contingency response.</b>	
<b>IID.1.1 Aim 1:</b> Observational Research, Clinical Trials and NIH Transplant Center	<p><b>Period 4 Activity:</b></p> <p>No Activity this period.</p>
<b>IID.1.2 Aim 2:</b> Research with NMDP Donors	<p><b>Period 4 Activity:</b></p> <p>The following activities have been completed on Dr. Switzer's Culture and Ethnicity Study:</p> <ul style="list-style-type: none"> <li>• 205 group 1 donors and 63 group 2 donors contacted for pre-consent</li> <li>• 147 group 1 donors and 52 group 2 donors enrolled in the study</li> <li>• 125 interviews completed</li> </ul>
<b>IID.1.3 Aim 3:</b> Expand Immuno-biology Research	<p><b>Period 4 Activity:</b></p> <p>The CIBMTR Immunobiology Working Committee (IBWC) met monthly during the quarter to discuss progress on ongoing research studies and review new proposals.</p> <ul style="list-style-type: none"> <li>• Three abstracts were submitted to the ASH annual meeting. All were accepted for oral presentations.</li> </ul>

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- Several study analyses were completed and manuscripts are under preparation.
- The IBWC leadership has been coordinating efforts with the leadership of the International Histocompatibility Working Group (IHWG) Hematopoietic Cell Transplant Component to provide data and sample support to the upcoming 15<sup>th</sup> International Histocompatibility Workshop.
- Eight new study proposals were received. Seven proposals were in support of IHWG studies and have been fast tracked through the committee to ensure data and/or samples are supplied in time for analysis prior to the Workshop in September 2008. Final review and approval of the proposals will be completed in the next quarter.

**Funding for CIBMTR IBWC studies:**

- The DNA extraction laboratory completed all contracted extractions. The receiving laboratory verified sample quality and has begun testing the samples.
- Two new funding requests were received for support of IHWG/IBWC studies and are currently under review for approval. Both requests would provide technician and reagent support to ensure timely completion of sample testing prior to the 15<sup>th</sup> Workshop.



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## ACRONYM LIST

AABB	American Association of Blood Banks	ICRHER	International Consortium for Research on Health Effects of Radiation
AML	Acute Myelogenous Leukemia	IS	Information Services
ARS	Acute Radiation Syndrome (also known as Acute Radiation Sickness)	IT	Information Technology
ASBMT	American Society for Blood and Marrow Transplantation	IRB	Institutional Review Board
ASHI	American Society for Histocompatibility and Immunogenetics	KIR	Killer Immunoglobulin-like Receptor
B-LCLs	B-Lymphoblastoid Cell Lines	NCI	National Cancer Institute
BMT CTN	Blood and Marrow Transplant - Clinical Trials Network	MHC	Major Histocompatibility Complex
C&A	Certification and Accreditation	MICA	MHC Class I-Like Molecule, Chain A
CBMTG	Canadian Blood and Marrow Transplant Group	MICB	MHC Class I-Like Molecule, Chain B
CBB	Cord Blood Bank	MUD	Matched Unrelated Donor
CBC	Congressional Black Caucus	NCBM	National Conference of Black Mayors
CBS	Canadian Blood Service	NIH	National Institutes of Health
CBU	Cord Blood Unit	NIMS	National Incident Management System
CHTC	Certified Hematopoietic Transplant Coordinator	NK	Natural Killer
CIBMTR	Center for International Blood & Marrow Transplant Research	NMDP	National Marrow Donor Program
CLIA	Clinical Laboratory Improvement Amendment	NRP	National Response Plan
CME	Continuing Medical Education	NST	Non-myeloablative Allogeneic Stem Cell Transplantation
CREG	Cross Reactive Groups	OCR/ICR	Optical Character Recognition/Intelligent Character Recognition
CT	Confirmatory Testing	OIT	Office of Information Technology
CTA	Clinical Trial Application	OMB	Office of Management and Budget
DIY	Do it yourself	ONR	Office of Naval Research
DKMS	Deutsche Knochenmarkspenderdatei	PBMC	Peripheral Blood Mononuclear Cells

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DMSO	Dimethylsulphoxide	PBSC	Peripheral Blood Stem Cell
DNA	Deoxyribonucleic Acid	PCR	Polymerase Chain Reaction
D/R	Donor/Recipient	PSA	Public Service Announcement
EBMT	European Group for Blood and Marrow Transplantation	QC	Quality control
EM	Expectation Maximization	RCC	Renal Cell Carcinoma
EMDIS	European Marrow Donor Information System	REAC/TS	Radiation Emergency Assistance Center/Training Site
FBI	Federal Bureau of Investigation	RFP	Request for Proposal
FDA	Food and Drug Administration	RFQ	Request for Quotation
Fst	Fixation Index	RITN	Radiation Injury Treatment Network
GETS	Government Emergency Telecommunications Service	SBT	Sequence Based Typing
GCSF	Granulocyte-Colony Stimulating Factor (also known as filgrastim)	SCTOD	Stem Cell Therapeutics Outcome Database
GvHD	Graft vs Host Disease	SG	Sample Group
HHS	Health and Human Services	SSP	Sequence Specific Primers
HIPAA	Health Insurance Portability and Accountability Act	SSOP	Sequence Specific Oligonucleotide Probes
HLA	Human Leukocyte Antigen	STAR®	Search, Tracking and Registry
HML	Histoimmunogenetics Mark-up Language	TC	Transplant Center
HR	High Resolution	TED	Transplant Essential Data
HRSA	Health Resources and Services Administration	TNC	Total Nucleated Cell
HSC	Hematopoietic Stem Cell	TSA	Transportation Security Agency
IBWC	Immunobiology Working Committee	URD	Unrelated Donor
IDM	Infectious Disease Markers	WMDA	World Marrow Donor Association
IHWG	International Histocompatibility Working Group	WU	Work-up
IND	Investigational New Drug		